

Remarks

Support for the Amendment and Status of the Claims

Support for the foregoing amendments to claims 169, 173, 177 and 193, and for new claims 196-198, can be found throughout the specification. Therefore, these amendments do not introduce new matter, and their entry and consideration are respectfully requested.

By the foregoing amendments, claims 169, 173, 177 and 193 are sought to be amended. Claims 166, 170 and 178 have been cancelled, and new claims 196-198 are sought to be added. Upon entry of the foregoing amendment, claims 1-16, 93-101, 106-107, 112-133, 138-159, 162, 164-165, 167, 169, 171, 173-175, 177, 181-186, 188 and 192-198 are pending in the application, with claim 1 being the sole independent claim. Claims 12-16, 93-101, 106-107, 112-133, 138-140, 142-159, 162, 165, 167, 171 and 175 have been withdrawn from consideration by the Examiner.

Summary of the Office Action

In the Office Action dated July 31, 2006, the Examiner has made one objection to, and two rejections of the claims. Applicants respectfully offer the following remarks to traverse each of these elements of the Office Action. Applicants respectfully request reconsideration of the present Application.

Objection to Claim 193

In the Office Action at pages 4-5, section 10, the Examiner has objected to claim 193 as being of improper dependent form for allegedly failing to further limit the subject matter of a previous claim. Applicants respectfully traverse this rejection. However, solely to expedite prosecution, present claim 193 recites "wherein the different substances are 61 kinases." Therefore, Applicants submit that present claim 193 further limits the subject matter of claim 1 from which it depends, and hence, is of proper dependent form. Applicants respectfully request that the Examiner reconsider and withdraw the objection to claim 193.

Rejection Under 35 U.S.C. § 112, First Paragraph

In the Office Action at pages 5-10, section 11, the Examiner has rejected claims 1-11, 141, 164, 166, 169, 170, 173, 177, 178, 181-186, 188 and 192-195 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

Applicants note that the Examiner has withdrawn the rejection of the claims under 35 U.S.C. § 112, first paragraph, made in the Office Action dated December 29, 2005, where the Examiner asserted that the rejected claims allegedly failed to comply with the written description requirement regarding kinases derived from any mammal or any Drosophila. Office Action at page 13, section 15. The Examiner has raised a new ground of rejection under 35 U.S.C. § 112, first paragraph, alleging that the rejected claims fail to comply with the written description requirement in view of

Vanhaesebroeck, *et al.*, *Exp. Cell Res.* 253:239-254 (1999) (hereinafter "Vanhaesebroeck").

The Examiner notes in the present rejection:

[T]he claims do not place any limitations on the number of atoms types of atoms or the way in which said atoms can be connected together to form such a compound or composition, i.e. the sequence similarity among the members of the claimed 61 different kinases or the shared structural motif of the claimed different functional kinase domains from the organism of '*mammal, yeast or Drosophila*'. Thus, virtually an infinite number of possibilities would be included in Applicants' claimed scope encompassing virtually every known class and subclass of compounds.

Office Action at page 6, last paragraph line 4, through page 7, line 4 (emphasis in original).

The Examiner further states that:

Although the large protein kinase superfamily are well characterized and known in the art such that the sequence of any kinases from any mammal, yeast and *Drosophila* can be determine[d] by bioinformatics tools and publicly available sequence information. . . . However, within the large protein kinase superfamily there are various different homologous proteins, i.e., substantial variation within the genus. . . . Consequently, the scope of the instant claimed compositions . . . includes an enormous number of structural variants.

Office Action at page 7, lines 4-18. The Examiner therefore concludes:

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variable, the instant specification single example is insufficient to describe the enormous genus.

Office Action at page 9, lines 7-10. Applicants respectfully disagree with the Examiner's contentions and conclusions.

As noted above, the Examiner has withdrawn the rejection under 35 U.S.C. § 112, first paragraph, set forth in the Office Action dated December 29, 2005. In fact, the Examiner now agrees that "the large protein kinase superfamily are well characterized and known in the art such that the sequence of *any* kinases from *any* mammal, yeast and Drosophila can be determine[d] by bioinformatics tools and publicly available sequence information." Office Action at page 7, lines 1-7 (emphasis added). The Examiner however maintains that because there is substantial variation within the genus of protein kinases, as allegedly evidenced by Vanhaesebroeck, the presently claimed invention does not meet the written description requirements of 35 U.S.C. § 112, first paragraph. Applicants respectfully disagree with the Examiner's assertions and conclusions.

As stated in Applicants' previously-filed replies dated September 19, 2005 and May 1, 2006 (the contents of which are incorporated by reference herein), the arguments presented by, and cases cited by, the Examiner do not support the conclusion that the present specification does not adequately describe the presently claimed invention. The claims at issue in the cases cited by the Examiner were directed towards novel DNA or protein *molecules themselves*, where the identity of the molecule was *unknown* prior to the filing date of the patents at issue, rather than methods or compositions *utilizing well-known and well-characterized classes of proteins*, as in the presently claimed invention.

The presently claimed invention is not directed to a compound or genus of protein kinases. Rather, present independent claim 1 is directed to "a positionally addressable array" which comprises protein kinases, or functional kinase domains thereof, positioned on a solid support. The presently claimed invention simply utilizes

protein kinases and/or functional kinase domains in the construction of an array, and is not directed to a nucleic acid or protein sequence, much less an *unknown, previously uncharacterized* nucleic acid or protein sequence, the focus of the subject matter of the case law cited by the Examiner. The claim terms here do not utilize "new or unknown biological materials that the ordinarily skilled artisan would easily miscomprehend." *See, e.g., Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332 (Fed. Cir. 2003), ("[the] Eli Lilly [decision] . . . [is] inapposite to this case because the claim terms at issue here are not new or unknown biological materials that ordinarily skilled artisans would easily miscomprehend."). Rather, the protein kinases and functional kinase domains for use in the presently claimed invention are all well-known, well-characterized proteins that the ordinarily skilled artisan would easily comprehend. *See, Amgen v. Hoechst*, 314 F.3d at 1332.

For example, in *Hanks, S.K. and Hunter, T., FASEB J.*, 9:576-596 (1995), the authors state that, as of 1995, "there are now hundreds of different members [of the kinase superfamily] whose sequences are known." *Hanks and Hunter*, page 576. Furthermore, kinases, for example serine kinases, were already readily recognized in 1995 by virtue of their conserved subdomains. *Hanks and Hunter*, page 576 (abstract). The Examiner has in fact acknowledged that "the large protein kinase superfamily are well characterized and known in the art such that the sequence of *any* kinases from *any* mammal, yeast and Drosophila can be determine[d] by bioinformatics tools and publicly available sequence information." Office Action at page 7, lines 1-7 (emphasis added). Furthermore, methods that could be used to confirm kinase activity were well known as of the filing date of the present application (*see e.g.*, Example 1 of present specification).

Thus protein kinases, and functional kinase domains thereof, were well-known in the art at the time of filing the present application.

While the Examiner has acknowledged that kinases from not only yeast, but also from *any* mammal or *any* Drosophila could be readily recognized at the time of filing of the presently claimed invention, it is noted that in some protein kinase subfamilies, there exist structural variants that do not share homology to one another. The Examiner therefore concludes that, because there allegedly exists substantial variation within the genus of protein kinases, the presently claimed invention does not sufficiently describe the claimed genus. Applicants respectfully disagree with the Examiner.

Applicants submit that, while Vanhaesebroeck may disclose protein kinase variants that have different structures and sequences, they are still *kinases*. This fact is readily apparent in Vanhaesebroeck at Figure 2 on page 241, where each of the PI3K's represented posses a "kinase core domain" (i.e., solid black oval). One of ordinary skill in the art, while recognizing that the proteins comprise different structures and homologies, would also recognize that each of the proteins are in fact kinases. Regardless of whether or not there exist structural variants within the protein kinase subfamily, all of these proteins are still "kinases," and would be readily recognized as such by the ordinarily skilled artisan.

As noted in Applicants' previously-filed replies, *Capon v. Eshhar* clarifies the written description requirement as delineated by *Fiers v. Revel*, 984 F.2d 1164, 1169 (Fed. Cir. 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 927 F.2d 1200 (Fed. Cir. 1991); and *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559 (Fed. Cir. 1997). 418 F.3d 1349, 1358 (Fed Cir. 2005). In discussing the current

state of the written description requirement under 35 U.S.C. §112, first paragraph, the Federal Circuit stated "[s]ince the law is applied to each invention *in view of the state of relevant knowledge*, its application will vary with differences in the state of knowledge in the field . . ." *Capon*, 418 F.3d at 1358 (Fed Cir. 2005) (emphasis added). In reviewing and overturning the Board's decision, the Federal Circuit held that "[t]he Board erred in refusing to consider the state of scientific knowledge . . ." *Id.* Furthermore, the Federal Circuit stated that the Board's reliance on *Eli Lilly, Fiers, Amgen v. Chugai* and *Enzo* for the case at bar was incorrect and explained that "[n]one of the cases to which the Board attributes the requirement of total DNA re-analysis, i.e., *Regents v. Lilly, Fiers v. Revel, Amgen [v. Chugai], or Enzo Biochem*, require a re-description of what was already known." *Id.* Applicants note that the Examiner has not addressed the controlling standard set forth in *Capon* as related to the present application in the most recent Office Action.

Furthermore, the Federal Circuit recently held in *Falko-Gunter Falkner v. Inglis*:

Indeed, a requirement that patentees recite known DNA structures, if one existed, would serve no goal of the written description requirement. . . nor would it be necessary to demonstrate to a person of ordinary skill in the art that the patentee was in possession of the claimed invention. . . Accordingly, we hold that where, as in this case, *accessible literature sources* clearly provided, as of the relevant date, gene and their nucleotide sequences . . . *satisfaction of the written description requirement does not require either the recitation of incorporation by reference (where permitted) of such genes and sequences*.

448 F.3d 1357, 1368 (Fed. Cir 2006) (emphasis added). Hence, the Federal Circuit has clearly stated that description of that which is well-known in the art is not required for satisfaction of the written description requirement of 35 U.S.C. § 112, first paragraph.

The Examiner states that "the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variable, the instant specification single example is insufficient to describe the enormous genus." Office Action at page 9, lines 6-9. Applicants respectfully submit that, contrary to the Examiner's assertion, Applicants have provided a description of the common attributes or characteristics that identify members of the genus utilized in the presently claimed invention -- they are all kinases. The ordinarily skilled artisan would readily recognize that proteins which posses a functional kinase domain, hence kinases, are encompassed by, and fully described by, the presently claimed invention in light of the state of the art at the time of filing of the present application.

Furthermore, the Examiner's reliance on *Fiddes v. Baird*, 30 USPQ2d 1481 (1993) is misplaced. The claims in *Fiddes* were directed to a "recombinant DNA molecule." *Id.* However, in the present case, and as in *Capon*, the presently claimed invention does not concern the discovery of gene function or structure. The proteins utilized in the present invention are a *known* class of proteins, kinases and functional kinase domains, with *known* functions. Even structural variants of kinases are readily recognized as *kinases* by the fact that such variants possess a kinase core domain. Describing every kinase or functional kinase domain, or every structural variant of a kinase, that can be used in the practice of the present invention would not add descriptive substance to the present application, and hence is not required under *Capon* or *Falko-Gunter Falkner* in order to meet the written description requirement of 35 U.S.C. § 112, first paragraph. *Capon*, 418 F.3d at 1357; *Falko-Gunter Falkner* 448 F.3d at 1368.

Applicants respectfully submit that the description in the present specification of at least one representative species of kinases or functional kinase domains (i.e., yeast kinases), especially when considering that the present invention is directed to positionally addressable arrays, not isolated kinases, satisfies the holding of *Lilly*, as clarified by *Capon*, and provides sufficient written description such that the ordinarily skilled artisan would determine that the inventors, at the time the application was filed, had full possession of the claimed invention. (*See also, Invitrogen Corp. v. Clontech Lab., Inc.*, 429 F.3d 1052, 1073 (Fed. Cir. 2005) holding that description of a single species is sufficient written description for claims directed to a modified polypeptide having DNA polymerase activity.)

As noted in Applicants' previously-filed reply, *Plowman et al., Proc. Natl. Acad. Soc.*, 96:13603-13610 (November 1999), discloses specific bioinformatics tools that were used to identify kinases from genomic information of *C. elegans* and assess publicly available expressed sequence tag data to identify 592 human kinases. (*Plowman et al., 13604, left column and Table 1*). Accordingly, using bioinformatics tools, such as those disclosed in *Plowman et al.* in conjunction with the publicly available sequence information, a skilled artisan would recognize that, as of the filing date of the present application, the sequences of virtually any kinase from any mammal or any *Drosophila*, including structural variants thereof, which must necessarily comprise a functional kinase domain, were either readily available or easily identifiable. Applicants assert, therefore, that the state of the art as of the filing date of the present application was such that one of skill in the art would be able to recognize a DNA sequence encoding a kinase or a kinase amino acid sequence from any mammal or any *Drosophila*, including

structural variations thereof, without further guidance from the present specification. Accordingly, Applicants believe that the present specification adequately and sufficiently describes the presently claimed subject matter in view of the state of the art at the time the application was filed. Reconsideration and withdrawal of this rejection are respectfully requested.

Rejection Under 35 U.S.C. § 103(a)

In the Office Action at pages 10-13, section 14, the Examiner has rejected claims 1-11, 141, 181-186, 188 and 192-195 under 35 U.S.C. § 103(a), as allegedly being unpatentable over Wagner *et al.* (U.S. Patent No. 6,329,209; hereinafter "Wagner") in view of Ashmarina *et al.* (*Eur. J. Biochem.* 149:67-72 (1985); hereinafter "Ashmarina") Applicants respectfully traverse this rejection.

The Examiner contends that Wagner discloses arrays of protein-capture agents and methods of making and using the arrays, and that the arrays comprise 100 or more different protein-capture agents per cm². The Examiner notes, however, that Wagner fails to disclose that the protein-capture agents are kinases. The Examiner relies on the disclosure of Ashmarina to cure this deficiency, stating that Ashmarina discloses immobilizing a yeast kinase onto a polymer substrate to screen for specific activity of monomeric enzyme.

The Examiner contends that it would have been obvious to combine the disclosure of Wagner with that of Ashmarina in order to generate the presently claimed invention. The Examiner asserts that one of ordinary skill in the art would have been motivated to combine the yeast kinase disclosed in Ashmarina with the array of Wagner

because of the advantage of providing a method of screening specific activity of monomeric enzyme, and since both references disclose immobilizing a protein onto a substrate. Therefore, the Examiner concludes that the presently claimed invention is rendered obvious. Applicants respectfully disagree with the Examiners' contentions and conclusions.

While Wagner may disclose arrays of protein-capture agents, Applicants respectfully submit, as the Examiner has noted, that Wagner clearly does not disclose arrays which comprise 61 kinases or functional kinase domains thereof *of an organism* selected from the group consisting of a mammal, yeast, and Drosophila, as recited in the presently claimed invention. The Examiner attempts to cure this deficiency by combining the disclosure of Wagner with that of Ashmarina, alleging that disclosure of a yeast kinase bound to a solid support provides sufficient motivation to generate the presently claimed invention. Applicants submit that the Examiner's attempt to combine these two disclosures in order to establish a *prima facie* case of obviousness fails for at least the following reasons.

First, while Ashmarina may disclose a *single* yeast kinase, phosphoglycerate kinase, this is the *only* kinase disclosed or even alluded to in Ashmarina. The presently claimed invention recites arrays which comprise at least *61 kinases or functional kinase domains thereof of an organism*. That is, the arrays of the present invention comprise at least 61 of the kinases of an organism. Disclosure of *one* kinase of an organism (yeast) by Ashmarina clearly does not provide sufficient disclosure or motivation for the ordinarily skilled artisan to be able to envision preparing arrays comprising *61 or more kinases of an individual organism*. Simply because Ashmarina may disclose

immobilization of glyceraldehyde-3-phosphate dehydrogenase on a solid support and then subsequent reaction with phosphoglycerate kinase, Ashmarina does not provide motivation to utilize this kinase to prepare the arrays disclosed in Wagner, much less the motivation required to prepare arrays comprising 61 kinases of an individual organism. Applicants submit that there is clearly no disclosure provided in Ashmarina that more than a single kinase of an organism could be attached to a substrate, let alone 61 kinases of an individual organism, as recited in the presently claimed invention.

Secondly, the Examiner states the following with regard to the alleged motivation to combine the disclosures of Wagner and Ashmarina:

[t]hus the type of substance immobilized on the surface of the substrate would be a *choice of experimental design* and is considered within the purview of the cited prior art. In addition, the specific type of kinase or functional kinase domains as claimed in claims 194 and 195 would be a *choice of experimental design* and is considered within the purview of the cited prior art.

Office Action at page 12, lines 18-22 (emphasis added). Applicants submit that the motivation set forth by the Examiner as "a choice of experimental design," is in fact, no more than an argument that it would have been *obvious to try* and prepare the arrays of Wagner with not only the single yeast kinase disclosed in Ashmarina. Applicants respectfully submit that, as set forth in M.P.E.P. § 2145.X.B., "obvious to try" cannot be used as a proper motivation for combining references under 35 U.S.C. 103(a) in an attempt to establish a *prima facie* case of obviousness.

"The admonition that 'obvious to try' is not the standard under § 103 has been directed mainly at two kinds of error. . . . In others, what was 'obvious to try' was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it."

In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (citations omitted).

M.P.E.P. § 2145.X.B., 2100-160. Applicants submit that, at best, Wagner and Ashmarina provide very general guidance as to the preparation of protein arrays. The Examiner's argument that it would be obvious to prepare the arrays of Wagner utilizing a yeast kinase as disclosed in Ashmarina is the epitome of "obvious to try" motivation, and one which can clearly not support a *prima facie* case of obviousness.

Moreover, even assuming that it may have been obvious to try and prepare the arrays of Wagner utilizing the *single* yeast kinase disclosed in Ashmarina, there is clearly no disclosure or motivation in either reference that would motivate one of ordinary skill in the art to prepare positionally addressable arrays comprising *61* kinases or functional kinase domains *of an organism*, as recited in the presently claimed invention. Disclosure of a single kinase of an organism which may be immobilized on a solid support, absent more, clearly cannot provide the motivation or reasonable expectation of success to prepare an array comprising at least 60 additional kinases or functional kinase domains of an organism.

In view of the foregoing remarks, Applicants respectfully submit that the disclosures of Wagner and Ashmarina, alone or in combination, cannot render obvious the presently claimed invention. Hence, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) are respectfully requested.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, rendered moot or otherwise overcome. Applicants therefore respectfully request that the

Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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